REMARKS

Claims 1-66 are pending in the application. Claims 19, 26-35, and 42-44 are amended herein without the addition of new matter. Claims 45 and 46 are cancelled herein, without prejudice. Claims 67-71are newly added, and do not introduce new matter. Claims 1-66 are subject to restriction to one of five groups:

Group I (claims 1-15, 17-18, and 65-66) alleged by the Office to be directed to methods for identifying genes responsible for high titer antibody production;

Group II (claim 16) alleged by the Office to be directed to a method of making a transgenic animal derived from a high titer antibody producing, inactivated mismatch repair fertilized egg cell;

Group III (claims 19-35 and 42-49) alleged by the Office to be directed to methods for modulating antibody production of cells;

Group IV (claims 36-41) alleged by the Office to be drawn to methods for selecting cells for high titer antibody production; and,

Group V (claims 50-64) alleged by the Office to be drawn to a host cell for the expression of antibody molecules comprising a defect in the expression of the monocyte polypeptide I and/or the alpha-1 antitrypsin gene.

Solely for the purpose of being fully responsive to the Office Action, Applicants provisionally elect the claims of Group III (19-35 and 42-49), provisionally elect subgroup "a" (dominant negative allele), provisionally elect subgroup "B" (claims 35 and 44-46, inactivation of alpha-1-antitrypsin), and provisionally elect cell type "i" (hybridoma). Applicants traverse the restriction requirement, and all requirements for further group restriction for the reasons detailed herein. Applicants expressly reserve the right to prosecute claims directed to non-elected subject matter at a later date.

For a restriction requirement to be proper, two requirements must be satisfied: (1) The inventions must be shown to be independent or distinct; and, (2) There must be a serious burden on the examiner (MPEP 803). Applicants respectfully submit that, at a minimum, Groups I and III should be rejoined because the inventions are not independent or distinct, and no serious burden on the examiner has been established. Groups I and III are not independent because there is a disclosed relationship, namely, that claims in Group I are

directed to the identification of genes responsible for high titer antibody production, and claims in Group III are directed to methods for producing high titer antibody production which comprise modulating the expression of genes responsible for antibody production, including those identified by the methods of group I. There is no serious burden on the examiner because a search relating to methods to identify genes responsible for high titer antibody production will likely reveal methods to modulate the expression of such genes, *i.e.*, confirmation of the identification of such genes may include the modulation of their expression.

Applicants respectfully submit that the restriction to one of the subgroups a-l is improper. Even if it is proper to restrict on the basis of the alleged distinction between nucleic acids and amino acids (and applicants are not conceding that it is), Applicants submit that subgroups a-g and l relate to nucleic acids, and j-k can include nucleic acids, and only h-i relate solely to compounds containing amino acids. Thus, at a minimum, a-g and j-l should be rejoined.

Applicants respectfully submit that the restriction to one of the subgroups A-F is also improper. Suppression and enhancement of antibody production are two sides of the same coin. The claimed methods are not distinct in that they describe methods to modulate antibody production, and thus whether the compounds inhibit or enhance the production, *i.e.*, the mode of operation of the compound is of no moment. As such, it would not be an undue burden to search generally on methods to modulate antibody production. The same holds true for the alleged distinction between alpha-1-antitrypsin and monocyte-activating polypeptide I.

Applicants respectfully submit that the restriction to one of the cell types i-vi is also improper. The cell types are not distinct in that they are antibody producing cells. Unsupported speculation that unique cellular environments may impose different effects on the efficiency of antibody production is not a proper basis for distinction. Similarly, whether a cell is immortalized or of primary origin is not a proper basis for distinction absent evidence that such would be expected to affect the relevant antibody producing genes. As no proper basis for restriction has been established, there is no undue burden on the examiner.

Applicants submit that the foregoing is fully responsive to the restriction requirement, and that all claims currently pending are in condition for allowance. Favorable

reconsideration of the restriction requirement, and a favorable action on the merits are earnestly requested.

The examiner is welcome to contact the undersigned at 215-564-8369 if the examiner believes a telephone interview would advance the prosecution in this case.

Respectfully submitted,

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